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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,210	07/08/2003	Michael S. Kopreski	00-1313-D	9776

7590 06/30/2006

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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/616,210	KOPRESKI ET AL.	
	Examiner	Art Unit	
	Frank W. Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *1-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group III, claims 21-36 in the reply filed on May 15, 2006 is acknowledged. The traversal is on the ground(s) that "[A]pplicants traverse restriction of claims 3-20 and 21-36 into Groups I and II in the instant Action. As set forth in the Action itself, these claims are both classified in class 435, subclass 91.51. Applicants respectfully submit that search and examination of all claims designated as belonging in Groups I and II in the Action would exert no undue hardship on the Office, since a search in the relevant classification area would necessarily identify any art relevant to the patentability of claims 3-28".

The above arguments have been fully considered and have not been found persuasive toward the withdrawal of the restriction requirement nor persuasive toward the relaxation of same such Groups II and III will be examined. First, the restriction is not based on the classification of Groups II and III but is based on that different and distinct searches are required for Groups II and III. For example, the search required for Group II such as 5T4 directed therapy in claim 15 is not required for Group III while the search required for Group III such as placenta in claim 24 is not required for Group II. Second, applicant has no evidence to show that a search in the relevant classification area would necessarily identify any art relevant to the patentability of claims 3-28. Therefore, the requirement is still deemed proper and is therefore made FINAL, and claims 21-36 will be examined.

Specification

2. The disclosure is objected to because of the following informalities since now case 09/155,152 is US Patent No.6,329,179, applicant is required to update this information in the first sentence of the specification.

Appropriate correction is required.

Claim Objections

3. Claims 21, 24, 30, and 34 are objected to because of the following informality: "an product fragment" in step b) should be "product fragment".

4. Claim 21 is objected to because of the following informality: "a woman post-partum" should be "a post-partum woman"

Appropriate correction is required

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Enablement

Claims 21-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification to show detection of 5T4 RNA in serum or plasma of a pregnant woman, a post-partum woman or woman with an antecedent pregnancy so that trophoblast tissue and placenta disease or condition can be detected, monitored or evaluated as recited in claims 21-36. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether 5T4 RNA can be detected in serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy so that trophoblast tissue and placenta disease or condition can be detected, monitored or evaluated as recited in claims 21-36.

Claims 21-23 are directed to a method of detecting, monitoring or evaluating trophoblast tissue in a pregnant woman, a woman post-partum or woman with an antecedent pregnancy by detecting 5T4 RNA in serum or plasma of a pregnant woman, a post-partum woman or woman with an antecedent pregnancy. Claims 24-29 are directed to a method of monitoring the placenta during pregnant by detecting 5T4 RNA in serum or plasma of a pregnant woman. Claims 30-33 are directed to a method of detecting 5T4 RNA in a bodily fluid from a pregnant or post-partum

woman for detecting trophoblast RNA in a blood plasma or serum from a woman for detecting, monitoring or evaluating a placenta disease or condition by detecting 5T4 RNA in a bodily fluid of a pregnant woman or a post-partum woman. Claims 34-36 are directed to a method of detecting trophoblast RNA in a blood plasma or serum from a woman for detecting, monitoring or evaluating a placental tissue by detecting 5T4 RNA in serum or plasma fro, a woman. Although the specification teach to detect 5T4 mRNA in certain cancer patients such as breast and lung cancer patients (see the specification, pages 14-16), the specification does not provide a guidance to show detection of 5T4 RNA in serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy so that trophoblast tissue and placenta disease or condition can be detected, monitored or evaluated as recited in claims 21-36. First, although it is known in the art that human trophoblast tissue and placenta express high level of 5T4 (see table 1 in Southall et al., Br. J. Cancer, 61, 89-95, 1996), there is no evidence to show that 5T4 RNA can be detected in serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy. Furthermore, even we assume that 5T4 RNA can be detected in serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy, there is no evidence to show that 5T4 RNA detected in serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy must come from human trophoblast tissue or placenta so that trophoblast tissue or placenta disease or condition can be detected, monitored or evaluated as recited in claims 21-36. In additional, art search cannot find an art related to detect 5T4 RNA in serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy. Second, there is no evidence to show that 5T4 RNA can be detected in any kind of bodily fluid of a pregnant or

post-partum woman as recited in claims 30-33. Third, since claim 21 does not indicate that the amplified trophoblast RNA or cDNA product fragment or amplified signal in step c) is identical to a product fragment or amplified signal in step b) and claims 24, 30, and 34 do not indicate that the amplified 5T4 RNA or cDNA product fragment or amplified signal in step c) is identical to a product fragment or amplified signal in step b), it is unclear how to perform step c) of claims 21, 24, 30, and 34. Therefore, in view of teachings in the specification, it is unpredictable how the methods recited in claims 21-34 can be performed.

With above unpredictable factor, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether 5T4 RNA can be detected in serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 21-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 21 is rejected as vague and indefinite. Although claim 21 is directed to a method of detecting, monitoring or evaluating trophoblast tissue in a pregnant woman, a post-partum woman or woman with an antecedent pregnancy, there is no method step for detecting, monitoring or evaluating trophoblast tissue in the claim and the goal of the claim (see preamble

cannot be reached. Furthermore, it is unclear that RNA from blood plasma or serum in step a) of the claim is from a pregnant woman, a post-partum woman or a woman with an antecedent pregnancy or not. Please clarify.

10. Claim 24 is rejected as vague and indefinite. Although claim 24 is directed to a method of monitoring the placenta during pregnant pregnancy, there is no method step for monitoring the placenta in the claim and the goal (see the preamble of the claim) cannot be reached. Please clarify.

11. Claim 24 recites the limitation "the placenta" in the preamble of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no word "placenta" before "the placenta". Please clarify.

12. Claim 24 recites the limitation "the human" in step a) of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no word "human" before "the human". Please clarify.

13. Claim 26 is rejected as vague and indefinite. Since claim 24 is directed to a method of monitoring the placenta during a pregnancy by detecting 5T4 RNA, it is unclear how to detect gestational trophoblastic disease by detecting any kind of any kind of trophoblastic RNA which may not be 5T4 RNA. Please clarify.

14. Claims 22, 27, 31, and 35 are rejected as vague and indefinite because amplifiable RNA reporters are not an amplification reaction. Please clarify.

15. Claims 23, 28, 32, and 36 are rejected as vague and indefinite. Since ELISA detection is enzyme-linked immunosorbant assay, it is unclear how ELISA detection can include methods using biotinylated or otherwise modified primers, laser-induced fluorescence, Southern blot

post-partum woman as recited in claims 30-33. Third, since claim 21 does not indicate that the amplified trophoblast RNA or cDNA product fragment or amplified signal in step c) is identical to a product fragment or amplified signal in step b) and claims 24, 30, and 34 do not indicate that the amplified 5T4 RNA or cDNA product fragment or amplified signal in step c) is identical to a product fragment or amplified signal in step b), it is unclear how to perform step c) of claims 21, 24, 30, and 34. Therefore, in view of teachings in the specification, it is unpredictable how the methods recited in claims 21-34 can be performed.

With above unpredictable factor, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether 5T4 RNA can be detected in serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 21-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 21 is rejected as vague and indefinite. Although claim 21 is directed to a method of detecting, monitoring or evaluating trophoblast tissue in a pregnant woman, a post-partum woman or woman with an antecedent pregnancy, there is no method step for detecting, monitoring or evaluating trophoblast tissue in the claim and the goal (see preamble of the claim)

of the claim) cannot be reached. Furthermore, it is unclear that RNA from blood plasma or serum in step a) of the claim is from a pregnant woman, a post-partum woman or a woman with an antecedent pregnancy or not. Please clarify.

10. Claim 24 is rejected as vague and indefinite. Although claim 24 is directed to a method of monitoring the placenta during pregnant pregnancy, there is no method step for monitoring the placenta in the claim and the goal of the claim (see the preamble of the claim) cannot be reached. Please clarify.

11. Claim 24 recites the limitation "the placenta" in the preamble of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no word "placenta" before "the placenta". Please clarify.

12. Claim 24 recites the limitation "the human" in step a) of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no word "human" before "the human". Please clarify.

13. Claim 26 is rejected as vague and indefinite. Since claim 24 is directed to a method of monitoring the placenta during a pregnancy by detecting 5T4 RNA, it is unclear how to detect gestational trophoblastic disease by detecting any kind of any kind of trophoblastic RNA which may not be 5T4 RNA. Please clarify.

14. Claims 22, 27, 31, and 35 are rejected as vague and indefinite because amplifiable RNA reporters are not an amplification reaction. Please clarify.

15. Claims 23, 28, 32, and 36 are rejected as vague and indefinite. Since ELISA detection is enzyme-linked immunosorbant assay, it is unclear how ELISA detection can include methods using biotinylated or otherwise modified primers, laser-induced fluorescence, Southern blot

analysis, Northern blot analysis, reverse dot blot detection, or high-performance liquid chromatography. Please clarify.

16. Claim 34 is rejected as vague and indefinite. Although Claim 34 is directed to a method of detecting trophoblast RNA in a blood plasma or serum from a woman for detecting, monitoring or evaluating a placental tissue, there is no method step for detecting, monitoring or evaluating a placenta tissue in the claim and the goal the claim (see preamble of the claim) cannot be reached. Please clarify.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 24-36 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 24-36 and 39-41 of copending Application No.10/363,023. Although the conflicting claims are not identical, they

are not patentably distinct from each other because the examined claims in this instant application is either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Although claims 24-36 in this instant application are not identical to claims 24-36 and 39-41 of copending Application No. 10/363,023, claims 24-36 and 39-41 in copending Application No. 10/363,023 are directed to the same subject matter and fall entirely within the scope of claims 24-36 in this instant application. In other words, claims 24-36 in this instant application is anticipated by claims 24-36 and 39-41 of copending Application No. 10/363,023.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

19. No claim is allowed.

20. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

June 23, 2006

FRANK LU
PRIMARY EXAMINER